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Food and Drug Administration
12420 Parklawn Drive Room 1-23
Rockville, MD 20857



Docket No. 98N-1215
Proposed Rule: Foreign Establishment
Registration and Listing

Merck & Co., Inc., is a leading worldwide, human health product company, that invests more than \$1 Billion on Research and Development (R&D), annually. To remain competitive in the global market, Merck frequently uses multiple manufacturing sites worldwide for each of its products. For this reason, we are very interested in and well qualified to comment on this FDA Proposed Rule to require foreign establishments whose products are imported or offered for import into the United States to register with FDA. The proposal would also require foreign establishments to identify a United States agent and describes some of the agent's responsibilities.

General Comments

Merck foreign drug establishments are already in compliance with the spirit of the proposed rule. Foreign manufacturing sites have been registered on form FDA 2656 accompanied by a letter from the subsidiary authorizing Merck & Co., Inc., the parent company, to interact on the foreign subsidiary's behalf with the FDA. Although Merck agrees with the intent of the proposed rule to codify the practice already in place, we do have several comments and questions regarding the proposed rule that are noted below.

Specific Comments/Questions

1. With respect to the definition of "Commercial Distribution" under Section 207.3(a)(5) and the requirement as to who must register and submit a drug list under Section 207.20:
 - a) Are these requirements intended to include a foreign toll manufacturer who is merely supplying a bulk active drug for incorporation into a finished drug product by the actual NDA holder?

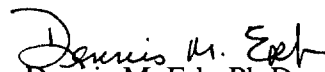
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- b) Does supplying under a toll arrangement for further processing by the NDA holder constitute "Commercial Distribution" requiring registration? If so, does this impose a greater obligation on a third party toller than on an affiliated company of the NDA holder, whose transfer or shipment of a bulk drug substance between affiliates does not constitute "Commercial Distribution"?
- c) Alternatively, could the toller's responsibility as bulk supplier to the NDA holder be documented and satisfied by requiring the NDA holder to list the foreign supplier in its NDA rather than requiring the foreign toller to separately register?
2. Supply of a bulk chemical intermediate by a foreign toller for incorporation into a finished drug product by the actual NDA holder apparently would not trigger these registration requirements because a bulk chemical intermediate would not be considered a drug. As a bulk intermediate and bulk drug substance are both further processed by the NDA holder, who then becomes fully responsible for the finished drug product that is commercially distributed, is there in fact a valid basis for requiring registration in one case and not in the other? A more appropriate alternative would be to list the foreign supplier in the NDA by the NDA holder in both cases.
3. With respect to Section 207.40(c)(2), in the case of a multi-national company with many foreign affiliates, it would be more appropriate to allow a person at the foreign affiliate to be listed as agent with a person at the U.S. parent listed as alternate agent if the foreign agent cannot be reached. This would make the communications between FDA and the foreign establishment under this section much more efficient and expeditious as the foreign affiliate person will be able to more directly answer questions about the foreign establishment's products and to more readily schedule inspections of the foreign establishment.
4. With respect to Section 207.40(c)(3), a 5-day timeframe to report changes in the foreign establishment's agent seems rather short and unnecessary, particularly if FDA accepts the approach of dual or alternate agents discussed in comment 3 above. We propose that this notification be increased to 14 calendar days or 10 business days.

We trust that these comments will be considered in further development of the proposed rule.

Sincerely,


Dennis M. Erb, Ph.D.
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